



DRAFT WORKING DOCUMENT FOR COMMENTS:

Procedure for prequalification of pharmaceutical products

Please submit your comments through the online platform, PleaseReview™ (<https://who.pleasereview.net/Main/Default.aspx?action=loadaddocument&reviewid=314>). If not registered or included in our mailing list, submit your request with full name, email address and organization/affiliation to nsp@who.int. For any technical questions, you may contact **Dr Luther Gwaza**, Team Lead, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications (gwazal@who.int), with a copy to, nsp@who.int. Comments should be submitted through the online platform by **02 June 2025**. Please note that only comments received by this deadline will be considered for the preparation of this document.

Our working documents are sent out electronically and uploaded into PleaseReview™. The working documents are also placed on the WHO Medicines website (<https://www.who.int/teams/health-product-and-policy-standards/standards-and-specifications/pharmaceuticals/working-documents-public-consultation>) under the "Working documents in public consultation". If you wish to receive all our draft guidelines, please send your full name, organization / affiliation, and email address to nsp@who.int and your name will be added to our electronic mailing list and review platform.

© World Health Organization 2025

All rights reserved.

This is a draft. The content of this document is not final, and the text may be subject to revisions before publication. The document may not be reviewed, abstracted, quoted, reproduced, transmitted, distributed, translated or adapted, in part or in whole, in any form or by any means without the permission of the World Health Organization

Please send any request for permission to: Ms Sinead Jones, Norms and Standards for Pharmaceuticals, Technical Standards and Specifications, Department of Health Products Policy and Standards, World Health Organization, CH-1211 Geneva 27, Switzerland, email: jonessi@who.int.

The designations employed and the presentation of the material in this draft do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this draft. However, the printed material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use. This draft does not necessarily represent the decisions or the stated policy of the World Health Organization.

SCHEDULE FOR DRAFT WORKING DOCUMENT QAS/25.974:

Procedure for prequalification of pharmaceutical products

Description of Activity	Date
Preparation of first draft working document.	Feb – March 2025
Mailing of working document to the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations (EAP) inviting comments and posting of the working document on the WHO website for public consultation.	April – May 2025
Consolidation of comments received and review of feedback. Preparation of working document for discussion.	June – July 2025
Discussion of the feedback received on the working document at the informal consultation on regulatory guidance for multisource products.	TBC
Preparation of a working document for discussion and possible adoption by the ECSPP	September 2025
Presentation to the Fifty-ninth meeting of the ECSPP.	13-17 October 2025
Any other follow-up action as required.	TBC

Procedure for prequalification of pharmaceutical products

Table of contents

1.	Introduction	4
2.	Glossary	4
3.	Purpose and principles.....	6
4.	Steps of the procedure	7
5.	Invitation for expressions of interest.....	9
6.	Data and information to be submitted.....	10
7.	Screening of dossiers submitted.....	12
8.	Dossier assessment.....	12
9.	Site inspection.....	13
10.	Reporting and communication of the results of the evaluation	14
11.	Outcome of the prequalification procedure.....	16
12.	Maintenance of prequalification status	17
13.	Cost recovery	19
14.	Confidentiality undertaking	19
15.	Conflict of interest	19
	Appendix 1	21
	Appendix 2	23

1. Introduction

The World Health Organization (WHO) provides United Nations agencies with advice on the acceptability, in principle, of pharmaceutical products for procurement by such agencies.

This activity of WHO aims to facilitate access to priority essential medicines that meet WHO-recommended norms and standards of acceptable quality. WHO undertakes a comprehensive evaluation of the quality of pharmaceutical products, based on information submitted by the manufacturers of such products or other applicants, and on an inspection of the corresponding manufacturing facilities and clinical sites. This is done through a standardized procedure which is based on WHO-recommended quality standards. The quality of pharmaceutical products is obviously crucial for the safety and efficacy of such products.

The pharmaceutical products found to meet the WHO-recommended quality standards are included in the list of medicines, as manufactured at the specified manufacturing sites, which are considered to be acceptable, in principle, for procurement by United Nations agencies. The list of prequalified pharmaceutical products is principally intended for use by United Nations agencies – including the Joint United Nations Programme on HIV/AIDS (UNAIDS), United Nations Children's Fund (UNICEF) and United Nations Population Fund (UNFPA) – to guide their procurement decisions. The growing list of pharmaceutical products that have been found to meet WHO-recommended standards may, however, also be of interest to other organizations and countries wishing to engage in the bulk procurement of pharmaceutical products.

Inclusion in the list does not imply any approval by WHO of the pharmaceutical products and manufacturing sites in question (which is the sole prerogative of national authorities).

Moreover, inclusion in the list does not constitute an endorsement or warranty by WHO of the fitness of any product for a particular purpose, including its safety and/or efficacy in the treatment of specific diseases.

2. Glossary

The definitions given below apply to the terms used in this procedure. They may have different meanings in other contexts.

active pharmaceutical ingredient (API)

A substance used in a finished pharmaceutical product (FPP), intended to furnish pharmacological activity or to otherwise have direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or to have direct effect in restoring, correcting or modifying physiological functions in human beings.

applicant

The person or entity who, by the deadline mentioned in the invitation, submits an expression of interest (EOI) to participate in this procedure in respect of the product(s) listed in the invitation, together with the required documentation on such product(s).

contract research organization (CRO)

An organization (commercial, academic or other) to which an applicant may have transferred some of its tasks and obligations in relation to the conduct of clinical studies with the product submitted to WHO for assessment under the current procedure.

finished pharmaceutical product (FPP)

A finished dosage form of a pharmaceutical product, which has undergone all stages of manufacture, including packaging in its final container and labelling.

invitation for expressions of interest (EOIs) or invitation

Invitation calling upon interested parties (e.g. manufacturers or other applicants) to submit an expression of interest (EOI) to WHO by a specified deadline for the purpose of participating in the WHO prequalification procedure in respect of the product(s) listed in the invitation. Such an EOI should be accompanied by the required documentation on the product(s) in question.

manufacturer

A company that produces, packages, repackages, labels and/or relabels pharmaceutical products.

pharmaceutical product

Any substance or combination of substances marketed or manufactured to be marketed for treating or preventing disease in human beings, or with a view to making a medical diagnosis in human beings, or to restoring, correcting or modifying physiological functions in human beings.

prequalification

Standardized quality assessment procedure of WHO to evaluate the acceptability, in principle, of pharmaceutical products for purchase by United Nations agencies. Agencies using information resulting from the prequalification procedure should perform additional steps of qualification prior to purchasing, such as ensuring financial stability and standing of the supplier, ability to supply the required quantities, security of the supply chain, pre-shipment quality control and other related aspects.

WHO listed regulatory authority (WLA)

- A national or regional regulatory authority that has successfully completed assessment via the WHO Global Bench Marking Assessment Tool (GBT) at maturity level 4 and undergone the performance evaluation phase for publicly designating regulatory authorities as a WHO Listed Authority
- Only in relation to good manufacturing practices (GMP) inspections: a medicine regulatory authority that is a member of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) as specified at <http://www.picscheme.org>.

Maturity level 3 or 4 regulatory authority (ML3/ML4 NRA)

A national regulatory agency or regional regulatory network included in the WHO list of national regulatory authorities operating at maturity level 3 or 4 as benchmarked against the GBT

3. Purpose and principles

The purpose of this WHO procedure is to evaluate whether certain pharmaceutical products (considered by WHO to be vital for the prevention and treatment of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), tuberculosis, malaria and other diseases, or for reproductive health) meet the requirements recommended by WHO and are manufactured in compliance with current good manufacturing practices (hereinafter referred to as GMP).

This procedure established by WHO is based on the following principles:

- the medicines eligible for prequalification are listed in invitations for EOI published on the WHO web site
- a general understanding of the production and quality control activities of the manufacturer;

- assessment of pharmaceutical product data and information on safety, efficacy and quality submitted by the manufacturer, including product formulation, manufacture and test data and results;
- inspection of finished pharmaceutical product (FPP) and active pharmaceutical ingredient (API) manufacturing site(s) for compliance with GMP;
- inspection of clinical testing units or contract research organizations (CROs) performing clinical trials for compliance with current good clinical practices (hereinafter referred to as GCP) and current good laboratory practices (hereinafter referred to as GLP);
- reliance on the information supplied by WLAs and ML3/ML4 NRAs;
- random sampling and testing of pharmaceutical products supplied;
- handling of complaints and recalls reported to WHO; and
- monitoring of complaints from agencies and countries.

WHO may collaborate with national regulatory authorities (NRAs) regarding dossier assessments and inspections. Subject to the terms of section 4 below, the prequalification of a product may also be based on approval by WLA or an ML 3/ 4 NRA.

WHO recommends that applicants expressing interest in participation in the prequalification procedure inform the NRAs in the country of manufacture of their intention and request them to collaborate with WHO in the quality assessment process. It is recommended that applicants provide the NRAs with the necessary authorization to discuss the relevant product files with WHO representatives during dossier assessment and site inspections (subject to appropriate confidentiality provisions, if necessary).

4. Steps of the procedure

WHO undertakes a comprehensive evaluation of the quality of pharmaceutical products, based on information submitted by the applicants, and inspection of the relevant manufacturing and clinical sites. (A flowchart showing the prequalification process is provided in Appendix 1.)

At regular intervals, and also taking into consideration pertinent input received from relevant United Nations agencies, WHO will publish an invitation to interested parties, requesting them to voluntarily participate in this procedure in respect of the products mentioned in the invitation.

By submitting an EOI, the applicant undertakes to share information with WHO on all relevant aspects of manufacture and control of the specified products along with changes made and/or planned. Interested applicants provide the necessary information to WHO by submitting a product dossier in the prescribed format, and other information as requested.

The procedure will normally include:

- assessment of product dossiers, which must include product data and information as specified in the guidelines for submission, available on the WHO web site
- inspection of manufacturing sites of FPPs and active pharmaceutical ingredients (APIs), to assess compliance with GMP;
- inspection of clinical sites (if applicable), to assess compliance with GCP and GLP as appropriate.

If the evaluation above demonstrates that a product and its corresponding manufacturing (and clinical) site(s) meet WHO-recommended standards, the product will be included in the list of pharmaceutical products that are considered to be acceptable, in principle, for procurement by United Nations agencies.

WHO reserves the right to terminate the evaluation of a specific product if the applicant is not able to provide the required information, and/or is unable to implement any corrective actions which WHO may require within a specified time period, or when the information supplied is inadequate to complete this procedure.

WHO recognizes the evaluation of relevant products by WLAs which apply standards for quality equivalent to those recommended by WHO. Provided that the NRA is willing to share certain information with WHO on the products in question, WHO will consider such products for inclusion in the list of WHO-prequalified products via an abridged pathway and according to the applicable submission guideline available on the prequalification web site. It will do so as and when information about such products becomes available to WHO and when the holders of the regulatory approval of such products express their interest in having these products prequalified by WHO. These products will be added to the list of products prequalified by WHO, on the basis of the scientific assessment and inspections conducted by the regulatory authority concerned, and the exchange of relevant information between the regulatory authority and WHO.

WHO acknowledges the evaluation of relevant products by ML3/ML4 NRAs which apply standards for quality equivalent to those recommended by WHO. Provided that the NRA is

willing to share certain information with WHO on the products in question, WHO will consider such products for inclusion in the list of WHO-prequalified products via a facilitated/reliance based¹ full assessment pathway and according to the applicable submission guideline available on the prequalification web site. It will do so as and when information about such products becomes available to WHO and when the holders of the regulatory approval of such products express their interest in having these products prequalified by WHO. These products will be added to the list of products prequalified by WHO, based on the complete dossier information submitted by the applicant and the scientific assessment and inspections conducted by the regulatory authority concerned, and the exchange of relevant information between the regulatory authority and WHO.

An inspection of a manufacturer or CRO may not be required if:

1. There has been an inspection by a WLA or ML3/ML4 NRA; and
2. The inspection was conducted within the last three years; and
3. Information on the inspection (including inspection report and responses to any deficiencies) is available for review by WHO; and
4. Based on this and other available information, it is determined² that the site(s) in question meet(s) the applicable WHO-recommended standards.

With a view to coordinating inspection activities, avoiding duplication and promoting information sharing without prejudice to the protection of any confidential and or proprietary information of the applicants and manufacturers in accordance with the terms of this procedure, WHO may disclose inspection related information to regulatory authorities of WHO Member States as well as to regulatory authorities that are members of the PIC/S.

5. Invitation for expressions of interest

The pharmaceutical products listed in an invitation for EOIs are considered by WHO to be vital for the effective treatment and prevention of the specified diseases (including HIV/AIDS, malaria and tuberculosis) or for reproductive health. These products are normally included in

¹ Such reliance on the work of the ML3/ML4 NRA could be partial, for example with respect to the quality assessment only or the safety/efficacy assessment only, or complete and cover all aspects of the dossier.

² Taking into account any known specific risk(s) associated with the product(s), the results of previous inspections conducted by WHO or a WLA or an ML3/ML4 NRA, any complaints (if known), the scope and detail of the inspection report, the number and type of any GMP deficiencies reported, the comprehensiveness of the manufacturer's response and the timelines for implementation of corrective action(s).

either the WHO Model List of Essential Medicines or the relevant WHO treatment guidelines and recommendations (or both).

The products included in the WHO Model List of Essential Medicines are those that satisfy the priority health-care needs of a population. They are selected, among other criteria, on the basis of disease prevalence, evidence on efficacy and safety, and analysis of comparative cost-effectiveness. Products included in WHO treatment guidelines are selected on the basis of an assessment of the evidence for benefits, risks, costs and appropriateness for use in a variety of situations, taking into account the needs of special populations and the values and preferences of the groups (professional and patient) using them.

Each invitation will be open and transparent, inviting all relevant parties to submit an EOI for the pharmaceutical products listed. Such an invitation will normally be published on the WHO web site and possibly also through other media, such as the international press.

In situations of high public health concern as determined by WHO, the Organization may also directly invite relevant parties to submit specified product dossiers for evaluation by WHO under this procedure without publication of an invitation for EOI.

6. Data and information to be submitted

Interested parties are expected to submit documentation on the pharmaceutical products as called for in the invitation for EOIs. Applicants should submit their product dossiers with the required information to the WHO focal point while the product remains invited,. Guidance and instructions developed for the submission of the dossiers are made available on the WHO web site.

Normally the applicants who participate in the WHO prequalification scheme for pharmaceutical products are the manufacturers of the FPPs, as specified in the invitations for EOIs. In the case that an applicant is not the manufacturer of the FPP, all relevant documentation, including (but not limited to) contract manufacturing documentation, should be submitted, demonstrating that the applicant is in full control of the manufacturing process for, and quality assurance of, the products submitted for prequalification.

In submitting an EOI for product evaluation, the applicant should send the following to the WHO focal point:

- a covering letter, expressing interest in participating in the WHO prequalification procedure and confirming that the information submitted in the product dossier is complete and correct;
- a product dossier, in the format specified in the WHO guidance documents on submitting product data and information;
- product samples, to enable visual examination and chemical and pharmaceutical analysis;
- a site master file (SMF) for each manufacturing site listed in the product dossier, in the format specified in the WHO guidance documents for submitting an SMF; and
- a contract research organization master file (CROMF) for each clinical site listed in the dossier, in the format specified in the WHO guidance documents for submitting a CROMF.

All documentation should be submitted in English.

For the purposes of this procedure, different requirements for documentation to be submitted apply to the following categories of products:

- multisource (generic) FPPs to be assessed by WHO;
- multisource (generic) FPPs approved by ML3/ML4 NRAs
- innovator FPPs approved by WLAs; and
- multisource (generic) FPPs approved by WLAs.

The documentation requirements for each of the above categories can be found on the WHO prequalification web site. These requirements may be revised from time to time.

Multisource generic products must be shown, either directly or indirectly, to be therapeutically equivalent to the comparator product if they are to be considered interchangeable. WHO will maintain and make public the list of comparator products for this purpose. The WHO web site provides guidance on the evidence needed for a product to be considered equivalent without the need for in vivo equivalence studies (i.e., application of biowaiver).

If considered necessary or desirable by either party, and before the actual evaluation process starts, a discussion may be held between the manufacturer and WHO. This meeting should be scheduled as early as possible with a predefined agenda to address questions sent in advance to WHO by the manufacturer.

7. Screening of dossiers submitted

Each product dossier submitted by an applicant will be screened for completeness before being evaluated. Dossiers submitted for products which are not listed in an invitation for EOIs or have not otherwise been invited by WHO will not be accepted for assessment.

Similarly WHO will not consider dossiers that are incomplete. The applicant will be informed that an incomplete dossier has been received and will be requested to complete the dossier within a specified time period. In the event of non-compliance, the dossier may be rejected on grounds of incompleteness.. Dossiers that are considered complete as the result of the screening will be retained by WHO for assessment.

After screening, if the dossier is accepted for assessment the applicant will be informed of this, including the dossier reference number, by letter. This letter will serve as an agreement between WHO and the applicant for the participation in prequalification and a commitment to comply with the provisions of the prequalification procedure.

8. Dossier assessment

The product information submitted in the dossiers will be assessed by teams of experts (assessors) appointed by WHO. The assessors involved in dossier assessment must have the relevant qualifications and experience in the fields of pharmaceutical development, quality assessment of pharmaceutical products, quality assurance, biopharmaceutics and other relevant fields. The assessors will be appointed in accordance with a standard operating procedure (SOP) established by WHO. The assessors should preferably be from NRAs and they will act as temporary advisers to WHO. The assessors must comply with the confidentiality and conflict of interest rules of WHO, as laid down in the relevant sections of this procedure.

The assessment of product dossiers will be done in accordance with SOPs established by WHO for that purpose so as to ensure uniformity in evaluation and timeliness of assessment activities. If needed, WHO may provide training to these experts.

Following the assessment of each part of the dossier, a report will be provided to the applicant. Applicants are expected to submit responses to comments and any additional information that

may be requested as soon as possible. Within a time stipulated for each deficiency letter, the applicant should submit responses to WHO addressing all queries. The procedure is usually suspended (i.e. WHO will not undertake any further action) until all required responses and any additional information is received by WHO.

Each applicant may request a hearing or meeting with the WHO experts involved in the assessment of this applicant's dossier to clarify issues identified by the WHO experts. WHO may provide technical assistance to applicants regarding appropriate product information to be submitted as well as production and control requirements.

9. Site inspection

WHO will plan and coordinate, in accordance with SOPs established by WHO and based on quality risk management (QRM) principles, the performance of inspections of the site(s) of manufacture of the API(s) and the FPP, and of the clinical testing units or CROs.

The following factors will be taken into account when planning inspections:

- the results of previous inspection(s) by WHO or aWLA or ML3 / ML4 NRA, and history of compliance of the company or facility with GMP, GCP and or GLP as appropriate;
- the outcome of the assessment of data submitted to WHO;
- complexity of the site, processes and product;
- number and significance of known quality defects (e.g. complaints, recalls);
- major changes to, e.g. buildings, equipment, processes, key personnel;
- site experience with manufacturing and testing of a product; and
- test results of official control laboratories.

The inspections of the manufacturing site(s) are conducted to assess compliance with GMP as recommended by WHO and include data verification. SMFs submitted by the applicant will be reviewed before an inspection is performed.

The inspections of clinical testing units or CROs are carried out to assess compliance with GCP and GLP, and to perform data verification.

The WHO norms and standards applicable to inspections of APIs and FPPs, and of clinical testing units or CROs, can be found on the WHO web site. These requirements may be revised from time to time.

The inspections will be performed by a team of inspectors usually including experts appointed by WHO, preferably from NRA inspectorates, who will act as temporary advisers to WHO. The inspectors must have the relevant qualifications and experience to perform such inspections, be competent in areas such as production and quality control of pharmaceuticals, and have appropriate experience in GMP and GCP or GLP. The inspectors must comply with the confidentiality and conflict of interest rules of WHO, as laid down in the relevant sections of this procedure. If needed, WHO may provide training to these experts.

A WHO staff member will coordinate the team and will normally lead the inspection team. Each team will perform the inspections and report its findings to WHO in accordance with SOPs established by WHO for that purpose so as to ensure a standard harmonized approach. A representative of the NRA of the country of manufacture would normally be expected to accompany the team to the manufacturing and testing facilities to assess the compliance with GMP and GCP or GLP.

In accordance with SOPs established by WHO and based on QRM principles, an on-site inspection by a WHO inspection team may be waived provided that the site in question is found to meet the applicable WHO-recommended standards following a desk review of requested inspection reports, the manufacturers response(s) to the relevant inspectorate describing corrective actions to any deficiencies identified in the inspection reports and an acceptable product quality review report for the identified product(s).

10. Reporting and communication of the results of the evaluation

Each assessment and inspection team will finalize its reports according to the established WHO SOP and format, describing the findings and including recommendations to the applicant, manufacturer(s) and/or CROs where relevant.

The findings from the dossier assessment including, but not limited to, deficiencies of the documentation and data submitted, shall be communicated in writing to the applicant requesting submission of the missing data and information, as appropriate.

The inspection report will be communicated to the manufacturer or CRO as applicable. With the written agreement of the manufacturer or CRO, a copy of the inspection report may also be provided to the applicant (if other than the manufacturer or CRO). If any additional information is required, or corrective action has to be taken by the manufacturer or CRO, WHO will postpone its decision on the acceptability of the site(s) concerned until such information has been evaluated or the corrective action has been taken and found satisfactory in light of the specified standards.

WHO reserves the right to terminate this procedure for a specific product if the applicant is not able to provide the required information or implement the corrective actions within a specified time period, or if the information supplied is inadequate to complete this procedure.

In the event of any disagreement between an applicant and WHO, an SOP established by WHO for the handling of such disagreements will be followed to discuss and resolve the issue.

As WHO is responsible for the prequalification procedure, the ownership of the reports lies with WHO. Thus, WHO shall be entitled to use and publish such reports subject always, however, to the protection of any commercially sensitive confidential information of the applicant, manufacturer(s) and/or testing organization(s). "Confidential information" in this context means:

- confidential intellectual property, know-how and trade secrets (including, e.g. formulas, processes or information contained or embodied in a product, unpublished aspects of trade marks, patents, etc.); and
- commercial confidences (e.g. structures and development plans of a company).

Provisions of confidentiality will be contained in the exchange of letters, to be concluded before the assessment of the product dossier or inspection of the manufacturing and clinical sites, between WHO and each applicant, manufacturer or CRO.

Notwithstanding the foregoing, WHO reserves the right to share the full assessment and inspection reports with the relevant authorities of any interested Member State of the Organization and interested United Nations agencies.

483

484 **11. Outcome of the prequalification procedure**

485

486 Once WHO is satisfied that this procedure is complete for the relevant product, and that the
487 WHO-recommended standards are met, the product, as manufactured at the specified
488 manufacturing site(s), will be included in the list of prequalified pharmaceutical products. The
489 list of prequalified pharmaceutical products will be compiled in accordance with an SOP
490 established by WHO for final decision-making on inclusion in the list. The list will be published
491 on the WHO web site and will specify the characteristics of the prequalified pharmaceutical
492 products, as described in Appendix 2 to this procedure.

493

494 Each applicant will receive a letter of prequalification from WHO informing it of the outcome of
495 the quality assessment process in regard of the submitted product(s). Once the product(s) are
496 included in the list of prequalified pharmaceutical products, the applicant shall be responsible
497 for keeping WHO continuously updated on all relevant aspects of the manufacture and control
498 of such product(s) and to meet any requirements, as agreed with WHO.

499

500 In accordance with World Health Assembly Resolution WHA57.14 of 22 May 2004, WHO will –
501 subject to the protection of any commercially sensitive confidential information – publish WHO
502 Public Assessment Reports (WHOPAR(s)) on the product dossier assessments and WHO Public
503 Inspection Reports (WHOPIR(s)) on the manufacturers and CROs, that were found to be in
504 compliance with WHO-recommended guidelines and standards. These reports will be published
505 on the WHO web site. Subject always to the protection of commercially sensitive confidential
506 information, WHO shall also be entitled to publish negative evaluation outcomes in accordance
507 with SOPs established by WHO. These include notices of concern as well as notices of
508 suspension.

509

510 The decision to list a pharmaceutical product is made based upon information available to WHO
511 at that time, i.e. information in the submitted dossier and on the status of GMP, GLP and GCP at
512 the facilities used in the manufacture and testing of the product at the time of the site
513 inspection(s) conducted by WHO or at the time of the site inspection(s) conducted by a WLA or
514 ML3/ML4 NRA, the outcome of which has been determined by WHO to meet the applicable
515 WHO-recommended standards, in accordance with the terms of this procedure. This decision is
516 subject to change on the basis of new information that may become available to WHO. If
517 serious safety and/or quality concerns arise in relation to a prequalified product, WHO may
518 delist the product after evaluation of the new evidence and a risk–benefit assessment, or may

suspend the product until results of further investigations become available and are evaluated by WHO.

12. Maintenance of prequalification status

Applicants are required to communicate details to WHO of any changes (variations) in manufacture and control that may have an impact on the safety, efficacy and quality of the product.

Guidance on variations to prequalified dossiers as can be found on the WHO web site.. These requirements may be revised from time to time.

It is the applicant's responsibility to provide WHO with the appropriate documentation (referring to relevant parts of the dossier) to prove that any intended or implemented variation will not have a negative impact on the quality of the product that has been prequalified. WHO will undertake an evaluation of variations according to the established WHO guidelines and SOPs and communicate the outcome to the applicant within the prescribed time lines. Adherence to the reporting requirements will be verified during the inspections carried out by WHO.

Random samples of prequalified products supplied by listed manufacturers or applicants will be taken for independent testing of final product characteristics. Certificates of analysis of final products released by the manufacturer and specifications for test methods should be provided by the manufacturer or applicant to WHO for review upon request. In the event of failure to meet the established criteria for testing, WHO will investigate the problem and communicate the outcome of this investigation to the manufacturer and applicant, if other than the manufacturer.

Complaints concerning prequalified pharmaceutical products communicated to WHO will be investigated in accordance with an SOP established by WHO for that purpose. After investigation, WHO will provide a written report of the problem and include recommendations for action where relevant. WHO will make the report available to the applicant/manufacturer, and to the NRA of the country where the manufacturing site is located. Subject always to the protection of commercially sensitive information as referred to above, WHO shall be entitled to make such reports public. In addition, WHO reserves the right to share the full report with the

relevant authorities of interested Member States of the Organization and interested United Nations agencies.

Manufacturers of prequalified pharmaceutical products and associated API manufacturers will be re-inspected at regular intervals as determined by WHO, but normally at least once every three years. Re-inspections are conducted to verify compliance with GMP as recommended by WHO and include data verification.

Furthermore, in order to maintain their prequalification status, WHO will arrange for prequalified pharmaceutical products to be requalified at regular intervals.

Every five years from the date of prequalification, or when requested to do so by the WHO Prequalification of Medicines Programme, the holder of a prequalified product is required to submit data and information in relation to the product to WHO for assessment. The purpose of this assessment is to verify that the product conforms to information and data submitted in relation to prequalification, conforms to current norms and standards, and to verify the consistency of the quality of the product and its manufacturing process(es) over the identified period.

The procedure and guidelines on the requalification of prequalified products can be found on the WHO web site. These requirements may be revised from time to time. Re-inspection and/or requalification may also be performed:

- if any fraud or omissions by the applicant, manufacturer(s) of an FPP or API, or CROs in the initial assessment procedure or during the follow-up activities, become evident; and
- if WHO or any United Nations agency considers that a batch or batches of supplied prequalified pharmaceutical products are not in compliance with the specifications which were found to be applicable upon prequalification

If, as a result of re-inspection or requalification, it is found that a product and/or specified manufacturing site no longer complies with the WHO-recommended standards, such products and manufacturing sites may be suspended or removed from the list of prequalified pharmaceutical products. Failure of a manufacturer or applicant to participate in re-inspection or requalification (as applicable) may also lead to suspension or removal from this list.

13. Cost recovery

WHO reserves the right to charge for this procedure on a cost recovery basis.

14. Confidentiality undertaking

The assessors and inspectors will treat all information to which they will gain access during the assessments and inspections, or otherwise in connection with the discharge of their responsibilities in regard to the above-mentioned project, as confidential and proprietary to WHO or parties collaborating with WHO in accordance with the terms set forth below.

Assessors and inspectors will take all reasonable measures to ensure that confidential information:

- is not used for any purpose other than the assessment/inspection activities described in this document; and
- is not disclosed or provided to any person who is not bound by similar obligations of confidentiality and non-use as contained herein.

Assessors and inspectors will not, however, be bound by any obligations of confidentiality and non-use to the extent they are clearly able to demonstrate that any part of the confidential information:

- was known to them prior to any disclosure by or on behalf of WHO (including by manufacturers); or
- was in the public domain at the time of disclosure by or on behalf of WHO (including by manufacturers); or
- has become part of the public domain through no fault of theirs; or
- has become available to them from a third party not in breach of any legal obligations of confidentiality.

15. Conflict of interest

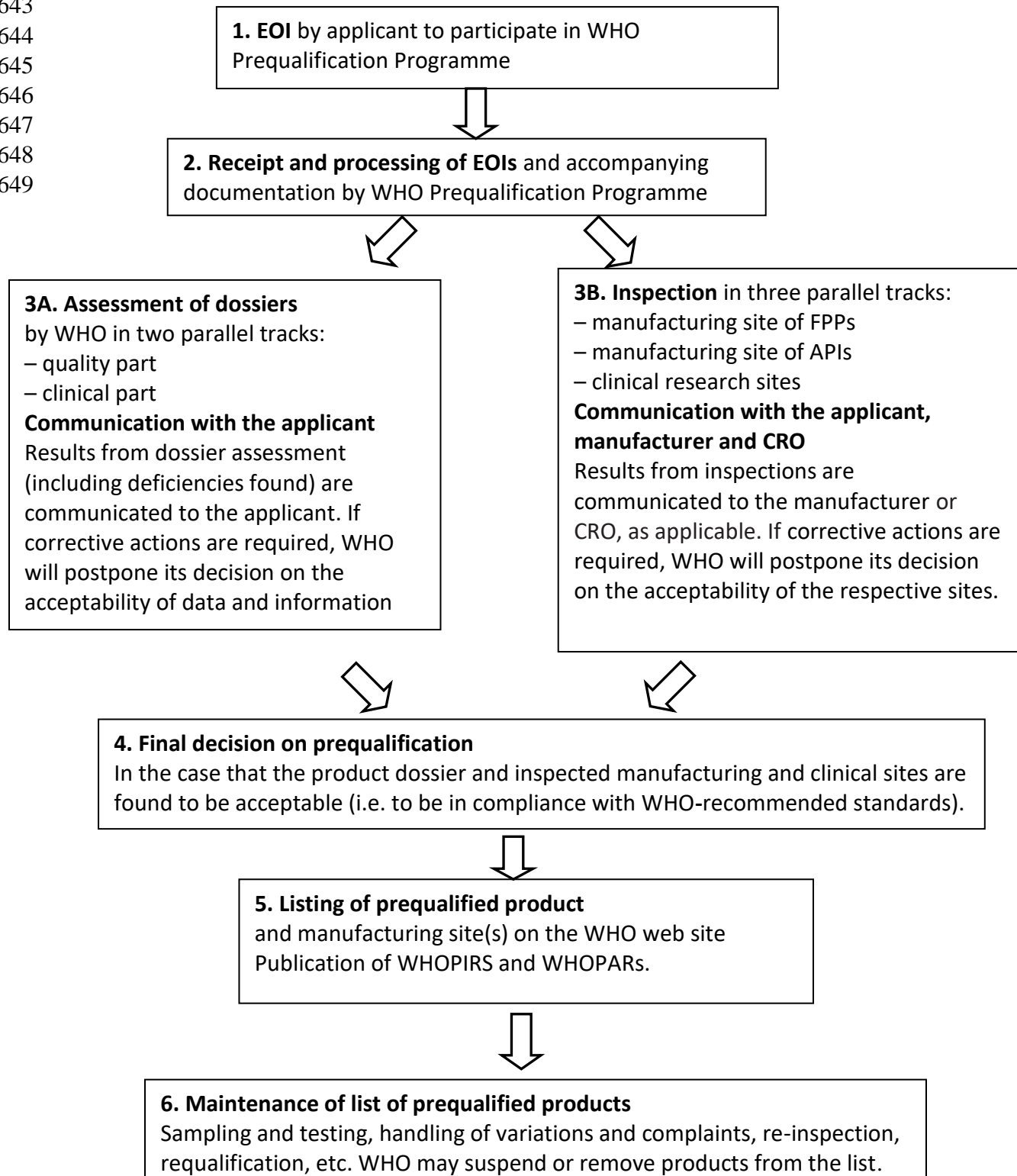
Before undertaking the work, each assessor and inspector will also (in addition to the above-mentioned confidentiality undertaking) be required to sign a declaration of interest. If, based on this declaration of interest, it is felt that there is no risk of a real or perceived conflict of

interest (or it is felt that there is only an insignificant and/or irrelevant conflict of interest), and it is thus deemed appropriate for the assessor or inspector in question to undertake this work, he/she will discharge his/her functions exclusively as adviser to WHO. In this connection, each assessor and inspector is required to confirm that the information disclosed by him/her in the declaration of interest is correct and complete, and that he/she will immediately notify WHO of any change in this information.

All inspectors furthermore agree that, at the manufacturer's or CRO's request, WHO will advise the manufacturer or CRO, in advance, of the identity of each inspector and the composition of the team performing the site inspection, and provide curricula vitae of the inspectors. The manufacturer or CRO then has the opportunity to express possible concerns regarding any of the inspectors to WHO before the visit. If such concerns cannot be resolved in consultation with WHO, the manufacturer or CRO may object to a team member's participation in the site visit. Such an objection must be made known to WHO by the manufacturer or CRO within 10 days of receipt of the proposed team composition. In the event of such an objection, WHO reserves the right to cancel all or part of its agreement with, and the activities to be undertaken by, that inspector.

Appendix 1

Flowchart of WHO prequalification of pharmaceutical products



650 EOI, expression of interest; FPP, finished pharmaceutical product; API, active pharmaceutical
651 ingredient; CRO, contract research organization; WHOPIR, public inspection report; WHOPAR,
652 public assessment report.

653

Appendix 2

Characteristics of the prequalified pharmaceutical product to be made available for public access on the WHO web site

- WHO product reference number
- International Nonproprietary Name (INN) of active pharmaceutical ingredient(s) (API(s))
- dosage form and strength
- trade name(s) of the product (if applicable)
- name of applicant and official address
- name of manufacturer of finished pharmaceutical product (FPP)
- physical address of manufacturing site(s) (and unit, if applicable)
- name of API manufacturer, physical address of manufacturing site(s) (and unit, if applicable)
- product description (as in FPP specifications, i.e. coated, scored, etc.)
- pack size(s), primary and secondary packaging material(s)
- storage conditions
- shelf-life (provisional, if applicable)
- summary of product characteristics
- package leaflet
- labelling